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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 08/955,373 | 10/21/1997 | SOREN MOURITSEN | BNIT0003-PCT-US | 7254 |

98994 7590 10/29/2012

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| EXAMINER | |
|---|---|
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 10/29/2012 | ELECTRONIC |

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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Application Number: 08/955,373
Filing Date: October 21, 1997
Appellant(s): MOURITSEN ET AL.

David Hoffman
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 6/22/12 and 6/11/12 appealing from the Office action mailed 2/15/12.

**(1) Grounds of Rejection to be Reviewed on Appeal**

Every ground of rejection set forth in the Office action dated 2/15/2012 from which the appeal is taken is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

The following ground(s) of rejection are applicable to the appealed claims.

Regarding appellants comments about the length of prosecution of the instant application, the instant application received a Final Rejection in May of 2000, after which appellants could have filed an Appeal Brief at any time.

**A)** Claims 102,103,105,111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 102 is indefinite in the recitation of "the secondary structure and tertiary structure of the self-protein is preserved to a large extent" because it is unclear what this means or encompasses. It is unclear what changes to the secondary and tertiary structure would or would not be encompassed by the aforementioned term. For example, it is unclear if this term encompasses changes at the physical/chemical level (e.g. crystal structure) or simply functional changes (e.g. still immunogenic antigen as evidenced by

antibody binding by antibodies specific for unmodified antigen). If the term is interpreted as encompassing changes at the physical/chemical level, it is unclear as to what deviations from the normal crystal structure would or would not be encompassed by the term “the secondary structure and tertiary structure of the pathogenic self-protein is preserved to a large extent”. It is unclear as to what changes to the secondary structure would or would not be encompassed by the aforementioned term. For example, it is unclear if this term encompasses changes at the physical/chemical level (egg. crystal structured) or simply functional changes (egg. still immunogenic antigen as evidenced by antibody binding by antibodies specific for unmodified antigen). If the term is interpreted as encompassing changes at the physical/chemical level, it is unclear as to what deviations from the normal crystal structure would or would not be encompassed by the term “the secondary structure and tertiary structure of the pathogenic self-protein is preserved to a large extent”. In addition, the phrase "large extent" is not defined in the specification and has no art recognized meaning in the context recited in the claims. Assuming arguendo that it was clear as to what changes were encompassed by preserving the secondary and tertiary structure, it would still be unclear as to what changes did or did not encompass a "large extent". The phrase "large extent" is not defined in the specification and has no art recognized meaning in the context recited in the claims.

**B)** Claims 102 is rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (US Patent 5,716,596) and Bona et al. (US Patent 5,969,109).

Russell-Jones et al. teach T cell epitopes derived from Trat protein (see Abstract). Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26 and Abstract). Russell-Jones et al. teach that the Trat peptide is inserted such that the protein still functions as an immunogen. The Trat peptide has been inserted into the immunogen in such a manner as to essentially preserve the overall secondary structure, because the ability of the immunogen to function as an immunogen is maintained (see page 8, first complete paragraph). Whilst the term "secondary and tertiary structure of the self-protein is preserved to a large extent" is indefinite as per above, for the purposes of this rejection it will be assumed the aforementioned limitation encompasses the ability of the immunogen to function as an immunogen is maintained. Russell-Jones et al. teach that the Trat modified immunogen can be used as a vaccine in a composition containing an adjuvant such as saponin (see page 8 and 13). Russell-Jones et al. teach that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 32 and page 31, first incomplete paragraph).

In addition, Bona et al. also teach that a T cell epitope can be substituted into a particular region of a target molecule wherein the T cell epitope retains immunogenicity (see column 11, second paragraph and column 4). Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12). Russell-Jones et al. teach that such vaccines can be used in animals and humans. Somatostatin is a "self protein" in view of its art recognized role in a variety of diseases (see Dean et al., column 2, first paragraph and column 6, third paragraph from bottom). Russell-Jones et al. do not teach use of the particular immunodominant foreign T cell epitopes recited in the claim. Russell-Jones et al. teach that immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art (see page 4, first paragraph). Russell-Jones et al. teach that diphtheria toxoid has already been approved for use as a carrier for human vaccines (see page 14, first paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Russell-Jones et al. teach the claimed method except for use of immunodominant foreign T cell epitopes derived from diphtheria toxoid, Bona et al. also teach that a T cell epitope can be substituted into a particular region of a target molecule wherein the T cell epitope retains immunogenicity, Russell-Jones et al. teach that immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art and that diphtheria toxoid was already approved as a carrier for human vaccines. One of ordinary skill in the art

would have been motivated to do so because immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art and diphtheria toxoid was already approved as a carrier for human vaccines.

**C)** Claim 111 is rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (US Patent 5,716,596) and Bona et al. (US Patent 5,969,109) as applied to claim 102 above, and further in view of Hellman (WO 93/05810) and Le et al. (US Patent 5,698,195).

The previous rejection renders obvious the claimed invention except for use of TNFα. Hellman teaches that modulation of self proteins responsible for manifestations of a particular disease can be achieved using self-protein conjugated to a carrier which is recognized by T helper cells(see pages 5-12) and wherein the administered hybrid molecule elicits antibodies against said molecule. Le et al. teach that antibodies against TNFα are used to treat TNFα mediated diseases in humans (see abstract and column 5).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the use of anti TNFα antibodies to treat TNFα mediated disease was known in the art, Hellman teaches that modulation of self proteins responsible for manifestations of a particular disease can be achieved by inducing antibodies against said molecules using self

molecules that contain T helper epitopes and Russell-Jones et al. teach methods for inducing antibodies against self proteins using Trat modified molecules.

**D)** Claims 103 and 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (US Patent 5,716,596) and Bona et al. (US Patent 5,969,109) as applied to claim 102 above, and further in view of Vitiello et al. (US 2003/0099634).

The previous rejection renders obvious the claimed invention except for use of the ovalbumin epitope recited in claim 105. Vitiello et al. disclose a peptide comprising said epitope wherein said epitope is a known immunogenic T cell epitope (see Example 7). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention using an immunogenic T cell epitope except for use of the particular peptide recited in the claim whilst Vitiello et al. disclose a peptide comprising said epitope wherein said epitope is a known immunogenic T cell epitope.

**(2) Response to Argument**

**A)** Claims 102,103,105,111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons elaborated above.

Regarding appellants comments about the interpretation of the aforementioned claim limitation in the context of prior art rejections, the MPEP section 2173.06 discloses that interpreting a term for prior art purposes does not preclude the rejection of said term under 35 USC 112, second paragraph as indefinite. Regarding the various submitted declarations related to the phrase under consideration, none of said declarations address the newly added limitation that the secondary and tertiary structure is "preserved to a large extent". Assuming arguendo that it was clear as to what changes were encompassed by preserving the secondary and tertiary structure, it would still be unclear as to what changes did or did not encompass a "large extent". The phrase "large extent" is not defined in the specification and has no art recognized meaning in the context recited in the claims. Regarding the first Travers declaration, said declaration addresses the phrase "essentially preserve the overall tertiary structure" wherein said phrase is not currently recited in the claims under consideration. Furthermore, Travers indicates that he would interpret said phrase as meaning:

*These 3 passages in my opinion clearly indicate to the skilled reader that "essential preservation of overall tertiary structure" implies that when a peptide containing a T-cell epitope is substituted into a self-protein according to the above-captioned patent application, the substitution is one which introduces a minimum of disturbance in the tertiary structure of the self-protein whereby a maximum number of B-cell epitopes are preserved when comparing to the unmodified self-protein.*

In the Delcayre declaration, Delcayre states:

*Based on the claim language as amended I understand that the secondary and tertiary structure of a self protein analog is essentially preserved where: (1) the self-protein analog induces an autoantibody response in a subject; and (2) the induced auto antibodies bind to the corresponding unmodified self-protein.*

In the Frokjaer declaration, Frokjaer states:

*In order to ascertain whether the tertiary structure of the self-protein has been preserved, thereby obtaining optimal therapeutic effects, screening procedures would be necessary. Such screening procedures would be routinely part of a drug development program's search for lead compounds and would be considered early on in the development phase to evaluate which modified self-proteins or self-protein analogs have preserved the tertiary structure of the original protein. Such procedures involve standard experimental techniques for which there are numerous publications. Reference is made to one in particular, which is used as a text book, on protein characterization, e.g. fluorescence spectroscopy, near U.V. circular dichroism, Fourier transformed infrared spectroscopy and multi-dimensional NMR techniques, namely, "Physical Methods to Characterize Pharmaceutical Proteins", Pharmaceutical Biotechnology, vol.7, Eds., J.N. Heron, W. Jisjoot & D.J.A. Crommelin, Plenum Press, New York, (1995). Ideally, for a screening process for lead compounds, two or more of*

*the above techniques would be carried out in order to evaluate whether there is a change in the tertiary structure of the protein.*

Thus, appellants **own declarants cannot agree as to what the phrases *"essential preservation of overall tertiary structure" or "essentially preserve the secondary structure and tertiary structure"* mean or *encompass*. *All three of the declarants have proffered different definitions as to what said phrase means.***

In addition, Frokjaer clearly indicates that said phrase encompasses actual measurement of the secondary and tertiary structure wherein Travers and Delcayre and applicants arguments clearly disagree with this assertion. Travers and Delcayre also have different definitions for the phrase under consideration.

Thus, it is clear that the limitation under consideration has no art recognized meaning. Regarding appellants comments, the fact that the analog induces an antibody response does not define what changes to the secondary and tertiary structure would or would not be encompassed by the aforementioned term. For example, the specification discloses that peptides fused to a carrier can elicit an antibody response wherein the peptides have no tertiary structure (see page 3 of specification, second section).

Furthermore, neither of said declarations address the newly added claim language that the secondary and tertiary structure are preserved to a "large extent". As per above it is unclear as to whether preservation of the secondary and tertiary structure encompasses

changes at the physical/chemical level (e.g. crystal structure) or simply functional changes (e.g. still immunogenic antigen as evidenced by antibody binding by antibodies specific for unmodified antigen). If the term is interpreted as encompassing changes at the physical/chemical level, it is unclear as to what deviations from the normal crystal structure would or would not be encompassed by the term “the secondary structure and tertiary structure of the pathogenic self-protein is essentially preserved”. It is unclear as to what changes to the secondary structure or tertiary structure would or would not be encompassed by the aforementioned term. Assuming arguendo that it was clear as to what changes were encompassed by preserving the secondary and tertiary structure, it would still be unclear as to what changes did or did not encompass a "large extent". The phrase "large extent" is not defined in the specification and has no art recognized meaning in the context recited in the claims.

The MPEP section 2173.05(a) [R-3] states:

*I. THE MEANING OF EVERY TERM SHOULD BE APPARENT*

*The meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed. Applicants need not confine themselves to the terminology used in the prior art, but are required to make clear and precise the terms that are used to define the invention whereby the metes and bounds of the claimed invention can be ascertained. During patent examination, the pending claims must be given the broadest reasonable interpretation consistent with the specification. In re Morris, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir.*

*1997); In re Prater, 415 F.2d 1393, 162 USPQ 541 (CCPA 1969). See also MPEP § 2111 - § 2111.01.*

*When the specification states the meaning that a term in the claim is intended to have, the claim is examined using that meaning, in order to achieve a complete exploration of the applicant's invention and its relation to the prior art. In re Zletz, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). The limitation under consideration is only recited in cited passage of the specification, page 3, wherein there is no definition of said term.*

Regarding the phrase under consideration, the meaning of said phrase is not apparent from the prior art or the specification. Appellants own declarants cannot even agree as to what said phrase means. The MPEP section 2173.02 states:

***2173.02 ** > Determining Whether Claim Language is Definite < [R-9]***

*> During prosecution, applicant has an opportunity and a duty to amend ambiguous claims to clearly and precisely define the metes and bounds of the claimed invention. The claim places the public on notice of the scope of the patentee's right to exclude. See, e.g., Johnson & Johnston Assoc. Inc. v. R.E. Serv. Co., 285 F.3d 1046, 1052 (Fed. Cir. 2002)(en banc). As the Federal Circuit stated in Halliburton Energy Services:*

*We note that the patent drafter is in the best position to resolve the ambiguity in the patent claims, and it is highly desirable that patent examiners demand that applicants do so in appropriate circumstances so that the patent can be amended during prosecution rather than attempting to resolve the ambiguity in litigation. Halliburton Energy Servs., Inc. v. M-I LLC, 514 F.3d 1244, 1255 (Fed. Cir. 2008).*

*A decision on whether a claim is indefinite under **35 U.S.C. 112**, second paragraph requires a determination of whether those skilled in the art would understand what is claimed when the claim is read in light of the specification. Power-One, Inc. v. Artesyn Techs., Inc., 599 F.3d 1343, 1350 (Fed. Cir. 2010); Orthokinetics, Inc. v. Safety Travel Chairs, Inc., 806 F.2d 1565 (Fed. Cir. 1986). In Orthokinetics, a claim directed to a*

*wheel chair included the phrase "so dimensioned as to be insertable through the space between the doorframe of an automobile and one of the seats thereof." Orthokinetics, 806 F.2d at 1568. The court found the phrase to be as accurate as the subject matter permits, since automobiles are of various sizes. Orthokinetics, 806 F.2d at 1576. "As long as those of ordinary skill in the art realized the dimensions could be easily obtained, § 112, 2d para. requires nothing more." Orthokinetics, 806 F.2d at 1576.*

*Claim terms are typically given their ordinary and customary meaning as understood by one of ordinary skill in the pertinent art, and the generally understood meaning of particular terms may vary from art to art. Therefore, it is important to analyze claim terms in view of the application's specification from the perspective of those skilled in the relevant art since a particular term used in one patent or application may not have the same meaning when used in a different application. Medrad, Inc. v. MRI Devices Corp., 401 F.3d 1313, 1318 (Fed. Cir. 2005).*

Regarding the phrase under consideration, the meaning of said phrase is not apparent from the prior art or the specification. Appellants own declarants cannot even agree as to what said phrase means.

Regarding appellants comments that the aforementioned declarations were not considered, the aforementioned declarations have been considered as per above.

**B)** Claim 102 is rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (US Patent 5,716,596) and Bona et al. (US Patent 5,969,109) for the reasons elaborated above.

Regarding appellants comments about antibodies to a self protein, Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26 and Abstract). ***Russell-Jones et al. teach that using***

***recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 32 and page 31, first incomplete paragraph).***

Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12). Russell-Jones et al. teach that such vaccines can be used in animals and humans. Somatostatin is a "self protein" in view of its art recognized role in a variety of diseases (see Dean et al., column 2, first paragraph and column 6, third paragraph from bottom). Thus, Russell-Jones et al. clearly teach the use of their invention to elicit antibodies (aka autoantibodies) to a self protein. With regards to reasonable expectation success, the prior art teaches/renders obvious the claimed invention and is therefore as enabled as the instant application.

Regarding appellants comments and the Legrand declaration, the MPEP section 716.01(b) states:

*Nexus Requirement and Evidence of Nonobviousness*

*TO BE OF PROBATIVE VALUE, ANY SECONDARY EVIDENCE MUST BE RELATED TO THE CLAIMED INVENTION (NEXUS REQUIRED)*

*The weight attached to evidence of secondary considerations by the examiner will depend upon its relevance to the issue of obviousness and the amount and nature of the evidence. Note the great reliance apparently placed on this type of evidence by the Supreme Court in upholding the patent in United States v. Adams, 383 U.S. 39,148*

*USPQ 479 (1966). To be given substantial weight in the determination of obviousness or nonobviousness, evidence of secondary considerations must be relevant to the subject matter as claimed, and therefore the examiner must determine whether there is a nexus between the merits of the claimed invention and the evidence of secondary considerations. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 305 n.42, 227 USPQ 657, 673-674 n. 42 (Fed. Cir. 1985), cert. denied, 475 U.S. 1017 (1986). The term "nexus" designates a factually and legally sufficient connection between the objective evidence of nonobviousness and the claimed invention so that the evidence is of probative value in the determination of nonobviousness. Demaco Corp. v. F. Von Langsdorff Licensing Ltd., 851 F.2d 1387, 7 USPQ2d 1222 (Fed. Cir.), cert. denied, 488 U.S. 956 (1988).*

The Legrand declaration discloses experiments performed using MVA-BN-HER2 which is a modified Vaccinia Ankara based recombinant vaccine vector derived from MVA-BN. The claimed invention is drawn to a method of inducing autoantibodies/treatment that **uses a peptide**. Thus, the disclosure of experiments performed using MVA-BN-HER2 is not commensurate in scope with the claimed invention which does not use a modified Vaccinia Ankara based recombinant vaccine vector. Furthermore, there is no disclosure in the specification of such vectors or the use of such vectors.

Mandl et al. disclose that the MVA-BN-HER2 vector induces immune responses that are not seen upon vaccination with protein antigen and wherein said responses are critical

to the results obtained when said vaccinia vector is administered (see Abstract). Thus, the results obtained in the Legrand declaration clearly depend on use of the MVA-BN-HER2 recombinant vaccinia vaccine vector wherein said vector is not the claimed invention or even an invention disclosed in the specification.

Mandl et al. teach that:

*In conclusion, the data presented here demonstrate that a single treatment with MVA-BN-HER2 was able to simultaneously induce Th1-dominated HER-2-specific immune responses and control tumor-induced immunosuppression resulting in potent anti-tumor efficacy. These preclinical results and the excellent safety profile and immunogenicity of MVA-BN even in immune-compromised patients (4–6) provide further support for the development of MVA-BN-HER2 for cancer immunotherapy.*

The responses to which Mandl et al. refers depend upon use of the MVA-BN vector, which is not the claimed invention. Furthermore, said vaccinia vector uses a modified tumor antigen wherein the use of tumor antigens is not disclosed in the specification. In addition, the elected species (aka TNFalpha) is not a tumor antigen.

Regarding appellants comments about TraT versus diphtheria toxoid and motivation, Russell-Jones et al. teach that immunodominant foreign T cell epitopes derived from diphtheria toxoid *were known in the art* and that diphtheria toxoid *was already approved as a carrier for human vaccines*. Furthermore the MPEP section 2123 [R-5] states:

*2123 [R-5] Rejection Over Prior Art's Broad Disclosure Instead of Preferred Embodiments*

*I. PATENTS ARE RELEVANT AS PRIOR ART FOR ALL THEY CONTAIN*

*"The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." In re Heck, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also > Upsher-Smith Labs. v. Pamlab, LLC, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005)(reference disclosing optional inclusion of a particular component teaches compositions that both do and do not contain that component);< Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed.").*

As per above, the cited reference constitutes art for all it discloses, not just the preferred embodiments. Furthermore, in KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL

1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill"**. However, in addition, one of ordinary skill in the art would have been motivated to do so because immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art and diphtheria toxoid was already approved as a carrier for human vaccines. Regarding appellants comments, Russell-Jones et al. teach Trat T cell epitopes are **inserted** into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26, page 31, lines 4-8, claim 14 and Abstract). Russell-Jones et al., page 31 discloses: **"the T cell epitope alone may be inserted within the protein antigen**". Regarding applicants comments about reasonable expectation of success, ***Russell-Jones et al. teach that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 32 and page 31, first incomplete paragraph).*** In addition, Bona et al. also teach that a T cell epitope can be **substituted** into a particular region of a target molecule wherein the T cell epitope retains immunogenicity (see column 11, second paragraph and column 4). Russell-Jones et al. teach that the Trat peptide is inserted such that the protein still functions as an immunogen. Regarding appellants comments about "self proteins", Russell-Jones et al. teaches that the claimed invention can be

used as a vaccine in humans (see page 33) and can be used to raise antibody responses against such proteins as luteinizing hormone, somatostatin, inhibin, FSH (e.g. ***self proteins***). Russell-Jones et al. teach that, "The at least one "immunogen" which forms part of the complex *is any molecule which it is desirable to use to raise an immune response*.". Regarding appellants comments about somatostatin, there is no evidence of record that the invention of Russell-Jones et al. lacks enablement regarding this particular embodiment. The prior art is considered enabled in the absence of evidence to the contrary. No such evidence has been provided by applicant. Regarding applicants comments about reasonable expectation of success, Bona et al. also teach that a T cell epitope can be **substituted** into a particular region of a target molecule wherein the T cell epitope retains immunogenicity and have produced such molecules. Regarding appellants comments, Russell-Jones et al. teach that their invention encompasses vaccines for use in animals and humans (see page 33). Russell-Jones et al. teach that one such immunogen could include luteinizing hormone or somatostatin or FSH or inhibin (see page 9). Said proteins could only be of two different origins (human or nonhuman). Thus, based on the disclosure of Russell-Jones et al., one of ordinary skill in the art would at once envisage use of human self-protein as a vaccine as per page 33 of Russell-Jones. Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26, page 31, lines 4-8, claim 14 and Abstract). Russell-Jones et al. teach that the Trat peptide is

inserted such that the protein still functions as an immunogen. Russell-Jones et al. teach that the Trat modified immunogen can be used as a vaccine in a composition containing an adjuvant such as saponin (see page 8 and 13). Russell-Jones et al. teach that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 31, first incomplete paragraph and claim 14 wherein the nucleic acid of claim 14 is used to recombinantly produce said protein). Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12). Russell-Jones et al. teach that such vaccines can be used in animals and humans.

One of ordinary skill in the art would have been motivated to combine the aforementioned teachings because immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art and diphtheria toxoid was already approved as a carrier for human vaccines. Furthermore, in the post KSR Int'l Co. v. Teleflex Inc. universe, motivation per se is not even required in a rejection under 35 USC 103. In KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill"**.

Regarding appellants comments about unexpected results, the TraT peptides and Diphtheria toxoid derived peptides taught by Russell-Jones et al. both stimulate T cells from random donors (aka are MHC unrestricted, see Table 3) and would therefore have the functional activities referred to in page 9 of the specification.

Regarding appellants comments about the scope of the claims, the claims are drawn to a method of administering a protein, not a vaccinia virus vector or any virus vector. Claim 102 clearly recites "administering to the subject an analog of the self-protein" and is limited to administration of a protein. The specification exclusively discloses administration of a protein in the claimed method. The administration of vaccinia vectors or any vector is not disclosed in the specification or original claims. The specification, page 10, last line indicates that " The vaccine according to the invention consists of one or more self-protein analogs modulated as described above and formulated with suitable adjuvants …". The claims do not recite or encompass use of a vaccinia virus vector. There is no disclosure in the specification or original claims of the administration of vaccinia virus vector or any virus vector in the claimed method. The specification and original claims only disclose use of an administered protein in the claimed methods. Appellants comments regarding this issue are not supported by any evidence of record.

Regarding the newly submitted supplemental materials from Mandl et al. (**which were not previously of record and were submitted with the instant Brief**), the data to which appellant refers is not encompassed by the instant invention. The claims

require administration of an "**analog of a self-protein**" to the subject. The "HER2 – CFA" referred to in the supplemental materials is a modified **human protein which is administered to mice** (see MANDL et al., page 19, second column, last section). **Thus, said modified protein is not a "self protein".** Furthermore, it is well known in the art that human proteins administered to mice invoke an immune response (aka mouse monoclonal antibodies which bind human molecules).

**Thus, the newly submitted supplemental materials from Mandl et al. disclose data that is not germane to the claimed invention.**

In addition, whilst said example is irrelevant to the claimed invention, Mandl et al. also disclose that the "HER2 + CFA" **had no activity in the tumor model which they used**.

Mandl et al. teach**: "More importantly, the quality of the immune response is a crucial factor in cancer immunotherapy as only treatment with MVA-BN®-HER2 resulted in protective anti-tumor immunity in this aggressive tumor model, while treatment with HER2+CFA did not."** (page 26, second column, continued on next page).

**C)** Claim 111 is rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (US Patent 5,716,596) and Bona et al. (US Patent 5,969,109) as applied to claim 102 above, and further in view of Hellman (WO 93/05810) and Le et al. (US Patent 5,698,195) for the reasons elaborated above.

Appellants comments are as addressed above.

In addition, regarding appellants comments about the number of cited references, the MPEP section 2145 V. states:

***V. ARGUING ABOUT THE NUMBER OF REFERENCES COMBINED***

*Reliance on a large* ***number of references*** *in a rejection does not, without more, weigh against the obviousness* ***of*** *the claimed invention. In re Gorman, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991) (Court affirmed a rejection* ***of*** *a detailed claim to a candy sucker shaped like a thumb on a stick based on thirteen prior art* ***references****.).*

**D)** Claims 103 and 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Dean et al. (US Patent 5,716,596) and Bona et al. (US Patent 5,969,109) as applied to claim 102 above, and further in view of Vitiello et al. (US 2003/0099634) for the reasons elaborated above.

Appellants comments are as addressed above.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Ron Schwadron/

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Conferees:

/DANIEL E. KOLKER/

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October 21, 2012